

In the Specification:

In accordance with the requirements of 37 C.F.R., § 1.821-1.825, please amend the specification by inserting the enclosed "SEQUENCE LISTING" immediately preceding the claims.

Please replace the Title with the following rewritten Title:

A1 --METHOD OF MAKING GLYCOPROTEIN EXHIBITING ERYTHROPOIESIS  
REGULATING ACTIVITY AND GLYCOPROTEIN PRODUCED BY THIS METHOD--

Please amend the specification by inserting a new section before the "Technical Field" as follows:

--CROSS REFERENCE TO RELATED APPLICATIONS

A2 This application is a continuation of application No. 08/466,412 filed June 6, 1995, which is a continuation of application No. 08/132,489 filed October 6, 1993, now U.S. Patent No 5,688,679, which is a continuation of application No. 07/453,381 filed December 18, 1989, now abandoned, which is a continuation of application No. 07/211,278 filed June 21, 1988, now abandoned, which is a continuation of application No. 06/879,423 filed June 27, 1986, now abandoned.--

Please replace the paragraph beginning at page 2, line 16, with the following rewritten paragraph:

A3 FIGURE 1 is a schematic representation of the subject 2426 bp Apa I restriction fragment that contains the human erythropoietin gene sequences (SEQ ID NO:1).

Please replace the paragraph beginning at page 3, line 13, with the following rewritten paragraph:

A4 Oligonucleotide mixtures were prepared using an Applied Biosystems synthesizer and end-labeled using <sup>32</sup>p-ATP and T4 polynucleotide kinase. The synthetic oligonucleotides

were designed to correspond to portions of the amino terminal amino acid sequence (SEQ ID NO:2) of:

H<sub>2</sub>N-Ala-Pro-?-Arg-Leu-Ile-Leu-Asp-Ser-Arg-Val-Leu-Glu-Arg-Tyr-Leu-Leu-  
Glu-Ala-Lys-Glu-Ala-Glu-?-Ile-Thr-Asp-Gly-Gly-Ala

24

174  
cont.

obtained by Yanagawa et al. (J.Biol.Chem. 259:2707-2710,1984) for the human protein purified from urine of patients with aplastic anemia. To reduce the degeneracy of the codons for the amino acid sequence of this region, the codon usage rules of Grantham et al. (Nucleic Acids Research 8:43-59, 1981) and Jaye et al. (Nucleic Acids Research 11:2325-2335, 1983) were employed. These rules take into account the relatively rare occurrence of CpG dinucleotides in DNA of vertebrates and avoid, where appropriate, potential A:G mismatch pairings. At amino acid position 24, an asparagine was placed as most likely (J.Biol.Chem. 259:2707-2710,1984). For the amino acids Glu-Ala-Lys-Glu-Ala-Glu-Asn (SEQ ID NO:3), 2 pools of 72 sequences each were synthesized to correspond to the predicted codons. Thus, one pool was TT(c/t)TC(a/g/t)GC(c/t)TC(c/t)TT(a/g/t)GCTTC (SEQ ID NO:4) for the 20 nucleotide probe, and the second pool replaced a T with a C at position 18. For the amino acids Glu-Asn-Ile-Thr-Asp-Gly (SEQ ID NO:5), one pool of sequences (AGC TCC TCC ATC AGT ATT ATT T[c/t]) (SEQ ID NO:6) was constructed for the 23 nucleotide probe.

In the Claims:

Please cancel claims 1-9, and add new claims 18-39 as follows:

175

18. (New) A method of making a glycoprotein exhibiting erythropoiesis regulating activity comprising:

culturing eukaryotic host cells transformed with a DNA construct comprising a eukaryotic promoter sequence operably linked to an insert consisting essentially of the sequence of SEQ ID NO:1 from position 59 through position 2204, the construct also including a 5' untranslated sequence located between the eukaryotic promoter and position 59, the 5'